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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/734,613      | 12/13/2000  | Marianne Bruggemann  | 37945-0009          | 3627             |

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EXAMINER

WEHBE, ANNE MARIE SABRINA

ART UNIT

PAPER NUMBER

1632

DATE MAILED: 12/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                        |                      |  |
|------------------------------|------------------------|----------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b> | <b>Applicant(s)</b>  |  |
|                              | 09/734,613             | BRUGGEMANN, MARIANNE |  |
|                              | <b>Examiner</b>        | <b>Art Unit</b>      |  |
|                              | Anne Marie S. Wehbe    | 1632                 |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 27 September 2004.  
 2a) This action is **FINAL**.      2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 35-62 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 35-62 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on 13 December 2000 is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>Notice to Comply</u> .                 |

## **DETAILED ACTION**

Applicant's amendment and response received on 9/27/04 has been entered.

Claims 35-62 are pending and under examination in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in previous office actions.

### ***Priority***

The certified copy of the GB 9823930.4 application as required by 35 U.S.C. 119(b) has been received by the office. Applicant's benefit of priority to the GB 9823930.4 application under 35 U.S.C. 119(b) is acknowledged.

### ***Claim Rejections - 35 USC § 103***

The rejection of claims 35-62 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,162,963 (12/19/00), filed on 6/5/95, and hereafter referred to as Kucherlapati et al., in view of Mendez et al. (1997) Nat. Genet., Vol. 15, 146-156 and Popov et al. (1996) Gene, Vo. 177, 195-201 is **withdrawn** in view of applicant's amendments to the claims and arguments.

Specifically, the applicant has amended independent claims 35 and 48 to include the limitation that the transgenic mouse comprises a YAC which contains at least a majority of the

human Ig V $\lambda$  genes of cluster A and all the human Ig J $\lambda$ -C $\lambda$  segments in germline configuration, and the limitation that the transgenic mouse has at least one endogenous  $\kappa$  light chain locus which is not disrupted. In view of this amendment, the claims are now deemed to be commensurate in scope with the evidence previously provided by the applicants for "unexpected results". Further, specifically in view of the added limitation that the transgenic mice have at least one endogenous  $\kappa$  light chain locus which is not disrupted, the examiner accepts the applicant's arguments concerning applicant's unexpected results in producing transgenic mice which contain the HuIg $\lambda$  YAC in their genome and which are  $\kappa^+/\kappa^-$  or  $\kappa^+/\kappa^+$  at the endogenous kappa locus, and which express light chains whose ratio of  $\kappa:\lambda$  is  $</= 60\% \kappa$  light chains and  $>/= 40\% \lambda$  light chains. While the cited art, in particular the teachings of Mendez et al., provide a reasonable expectation that transgenic mice made according to the teachings of Kucherlapati et al. using the YAC taught by Popov et al. which comprise a disruption in both endogenous kappa loci would show an approximately equal distribution of human kappa and human lambda light chain gene expression, the combination of the teachings of Kucherlapati et al., Mendez et al. and Popov et al. does not provide a reasonable expectation of success in generating an equal distribution of murine kappa and human lambda light chain gene expression in the presence of at least one undisrupted kappa locus in view of the art recognized preference for kappa light chain expression in mice which yields ratios of 95% kappa light chain and 5% lambda light chain in normal non-transgenic mice.

Applicant's amendments to the claims have resulted in the following new grounds of rejection.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 35-62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 35 and 48 have been amended to recite, “A transgenic mouse comprising a yeast artificial chromosome (YAC)....”. It is unclear from the claim as written whether the YAC is part of the germline of the transgenic mouse or whether the mouse simply contains a non-integrated YAC in some or all of the cells. **Amendment of the claims to recite “A transgenic mouse comprising in its genome a yeast artificial chromosome (YAC)....” would overcome this rejection.** Claims 36-47, and 49-62 depend on either claim 35 or claim 48 and are thus included in this rejection.

Claim 47 is indefinite in that the limitation recited in dependent claim 47 conflicts with the limitations in amended independent claim 35 from which claim 47 ultimately depends. Specifically, claim 35 has been amended to recite, “wherein at least one endogenous κ light chain locus of the transgenic mouse is not disrupted”. Transgenic mice produced according to claim 47 would include mice which could be κ<sup>-</sup>/κ<sup>-</sup>. Mice which are κ<sup>-</sup>/κ<sup>-</sup> conflict with the limitation in claim 35 that the mice have at least one endogenous κ light chain locus that is not disrupted. As such, the metes and bounds of the claims cannot be determined.

Claim 52 is indefinite in that the limitations recited in this dependent claim conflict with the limitations of amended independent claim 48 from which claim 52 depends. Specifically, claim 48 has been amended to recite, “wherein the YAC contains at least a majority of the human Ig V $\lambda$  genes of cluster A and all the human Ig J $\lambda$ -C $\lambda$  segments in germline configuration”. Claim 52 depends on claim 48 and recites, “wherein the mouse comprises a YAC of greater than 100Kb which contains a proportion of the human V $\lambda$  genes proximal to the J $\lambda$ -C $\lambda$  cluster in germline configuration”. As the YAC described in claim 52 only comprises a proportion of the human V $\lambda$  genes rather than a majority of the genes, it conflicts with the limitations of claim 48. Further, the limitation of claim 52 appears to be broader than claim 48 as a YAC comprising the majority at least a majority of the human Ig V $\lambda$  genes of cluster A and all the human Ig J $\lambda$ -C $\lambda$  segments in germline configuration is substantially greater than 100Kb. As such the metes and bounds of the claims cannot be determined.

Claim 62 is indefinite in that the limitation recited in dependent claim 62 conflicts with the limitations in amended independent claim 48 from which claim 62 ultimately depends. Specifically, claim 48 has been amended to recite, “wherein at least one endogenous  $\kappa$  light chain locus of the transgenic mouse is not disrupted”. Claim 62 depends ultimately on claim 48 and further recites, “wherein expression of the endogenous mouse heavy and/or light chain loci are prevented”. As such the mice claimed in claim 62 would include mice with a  $\kappa^+/\kappa^-$ . Mice which are  $\kappa^-/\kappa^-$  conflict with the limitation in claim 48 that the mice have at least one endogenous  $\kappa$  light chain locus that is not disrupted. As such, the metes and bounds of the claims cannot be determined.

The following formal matters are newly raised in this action.

***Nucleotide and/or Amino Acid Sequences***

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1 .821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1 .821 through 1 .825 for the reasons) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/or Amino Acid Sequence Disclosures. Specifically, Figure 5 contains multiple sequences which are not identified by SEQ ID NOS. Applicant is required to either 1) amend the brief description of Figure 5 on page 10 of the specification to include the appropriate SEQ ID NOS, or 2) amend the Figure to include the appropriate SEQ ID NOS. While the examiner notes that a CRF and paper copy of a sequence listing are present in the application, it is unclear whether the sequences present in Figure 5 are in fact present in the sequence listing. If such is the case, the applicant may simply amend either the specification or the drawings as indicated without filing a new sequence listing. However, if the sequences are not all present in the sequence listing on file in the instant application, a new sequence listing in paper form and CRF are required.

***Drawings***

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because **Figure 5 is not legible**. Applicant is advised to employ the services of a

competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

## **INFORMATION ON HOW TO EFFECT DRAWING CHANGES**

### **Replacement Drawing Sheets**

Drawing changes must be made by presenting replacement figures which incorporate the desired changes and which comply with 37 CFR 1.84. An explanation of the changes made must be presented either in the drawing amendments, or remarks, section of the amendment. Any replacement drawing sheet must be identified in the top margin as "Replacement Sheet" (37 CFR 1.121(d)) and include all of the figures appearing on the immediate prior version of the sheet, even though only one figure may be amended. The figure or figure number of the amended drawing(s) must not be labeled as "amended." If the changes to the drawing figure(s) are not accepted by the examiner, applicant will be notified of any required corrective action in the next Office action. No further drawing submission will be required, unless applicant is notified.

Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin.

### **Annotated Drawing Sheets**

A marked-up copy of any amended drawing figure, including annotations indicating the changes made, may be submitted or required by the examiner. The annotated drawing sheets must be clearly labeled as "Annotated Marked-up Drawings" and accompany the replacement sheets.

### **Timing of Corrections**

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in ABANDONMENT of the application.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. The examiner can be reached Monday- Friday from 9:30-6:00 EST. If the examiner is not available, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. For all official communications, **the new technology center fax number is (571) 273-8300**. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737.

Dr. A.M.S. Wehbé

ANNE M. WEHBE, PH.D.  
PRIMARY EXAMINER

